Editorial

Health economics and the search for shunt-responsive symptomatic hydrocephalus in the elderly

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It is now some 40 years since the triad of gait disturbance, cognitive decline, and urinary incontinence was first formally delineated, although unusual presentations of hydrocephalus had been previously noted.1 When such normal-pressure hydrocephalus (NPH) is caused by, for example, previous subarachnoid hemorrhage (SAH) or meningitis, the results of cerebrospinal fluid (CSF) diversion are excellent. Unfortunately, the situation is less clear-cut in idiopathic cases.11,17,18 One major problem is the overlap of clinical features, with conditions that would not be expected to respond to CSF diversion. Many elderly patients can have more than one of these conditions: CSF disturbance, subcortical vascular disease, and neurodegenerative processes including Alzheimer and Parkinson diseases. Hence, it is more realistic to look for a remediable hydrocephalic component to an elderly patient’s balance, walking, cognitive, and urinary control problems.

Clinically, the typical patient with shunt-responsive NPH will have problems with balance and gait initiation before cognitive decline, which is unlike Alzheimer disease. The subcortical pattern of dementia displayed in NPH is quite unlike Alzheimer disease but similar to subcortical ischemic dementia.9 The dementia in NPH follows two patterns: decline in frontal executive function followed by a more global dementia. Interestingly, the global dementia responds better to shunt insertion than does executive function.9 Some patients with ventriculomegaly are referred after they have failed to respond to anti-Parkinson therapy, some of whom have responded subsequently to the placement of a shunt.

If NPH was simply the result of a CSF flow disturbance, the effect of shunt insertion would depend on CSF outflow resistance, which it does in broad terms but with some exceptions that are not understood.5 Infusion studies are usually restricted to the more difficult cases, which inevitably reduces their specificity and sensitivity. It is important to emphasize that it is not sufficient simply to insert a shunt and then send the patient back to the referring physician. It is necessary to ensure that the shunt is draining CSF as intended. Changes in ventricle size are often subtle even in responders. Without preoperative CSF infusion studies, it is difficult to know whether CSF dynamics have been normalized. Extended lumbar CSF drainage has been advocated, but some patients who respond to a shunt do so only after some weeks so that there is a risk of false negatives with this test. There is also the cost of the hospital stay and the potential risk of infection. Mendelow’s lumbar subcutaneous shunt may help resolve this conundrum (http://www.nice.org.uk; IPG068).

The presence of white matter deep subcortical lesions (DSCLs) on magnetic resonance (MR) imaging with sulcal atrophy (not just widening of the sylvian fissures) reduces the probability of a successful outcome after shunt insertion but does not exclude it.6 Moreover, it appears that patients with such DSCLs have a greater risk of complications so that the risk–benefit ratio of shunt insertion is more evenly balanced.16 Recent study data have revealed that such DSCLs reflect ependymal loss, demyelination, arteriolar sclerosis, and amyloid angiopathy with tissue markers suggestive of a hypoxic environment. The overlap of NPH with subcortical ischemic disease is well known. Cerebral autoregulation in the deep white matter is impaired in NPH14 but much less globally. Hemispheric cerebrovascular reactivity is inversely related to CSF outflow resistance in patients presenting with the characteristic triad and ventriculomegaly.4 In summary, there are many different tests requiring various degrees of expertise and expense and none that alone has sufficient sensitivity and specificity. Hence, it is essential to consider all aspects of an individual case including clinical presentation, neuropsychological profile, MR imaging features, and some measure of intracranial dynamics.

There have always been advocates for simply inserting a shunt in patients suspected of having NPH. This policy was associated with a high rate of complications when fixed valves were used, but the advent of programmable valves
and a more meticulous approach to perioperative management has resulted in lower rates of complications. Is it now time to revisit “blind” shunt insertion without all the paraphernalia and expense of confirmatory tests?

Dr. Stein, of the well-respected Stein–Langfitt outcome scale for NPH, and his coworkers have taken on the challenge of applying the complex tools of health economics to the conundrum of shunt placement for dementia associated with ventriculomegaly in the elderly.\textsuperscript{4,16} In summary, they recommend offering a shunt to all patients suspected of having NPH without resorting to any screening tests except for simple scanning to confirm the presence of hydrocephalus. They argue that no screening test by itself is sufficiently specific and sensitive, such tests are expensive, progressive dementia is awful, the cost of long-term institutional care is high, and the risk–benefit ratio of modern shunt insertion is acceptably low. Even if shunt placement does not help, the number of patients who fare worse will be relatively small and at least everybody will have the sense that all potentially treatable causes have been addressed. Finally, the overall costs for the individual will have been minimized.

There is precedence for the practical application of health economics to neurosurgery, which started well before the present debate over the crisis in funding for health care worldwide.\textsuperscript{9} Neurosurgery in general is cost-effective as measured by cost per quality-adjusted life year (QALY),\textsuperscript{15} even for poor-grade SAH, for example.\textsuperscript{21} Oral nimodipine for the prophylactic treatment of delayed cerebral ischemia after SAH is highly cost-effective. Initially, the advent of programmable valves for NPH was met by concerns for their market price—very different from their production cost—but they are cost-effective nevertheless.\textsuperscript{22}

Unfortunately, many neurosurgeons may find it difficult to follow the process adopted in these two papers by Dr. Stein and colleagues.\textsuperscript{3,20} Decision trees, health utilities, and Markov modeling are not in the everyday vocabulary of the field of health economics argue as follows: \textsuperscript{14} “Economic evaluation of pharmaceuticals: Frankenstein’s monster or vampire of trials?”

Note the authors’ following assumptions: 1) The diagnostic criteria used for the inclusion of a published series are those accepted by Hebb and Cusimano\textsuperscript{3} in their systematic review; no distinction has been made among long-standing overt ventriculomegaly in adults, idiopathic cases, and vascular comorbidity. 2) Shunt-related complications are the same in shunt responders and nonresponders: this is probably not true. Patients with significant subcortical ischemia are more at risk of complications in general.\textsuperscript{10} 3) The annual mortality rate returns to normal in shunt responders: this is probably not true. The relative risk of death was 3.3 in successfully treated adult patients with hydrocephalus compared with healthy age-matched controls.\textsuperscript{10} 4) Health utilities have been based on the degree of dementia and not on the most common presenting problem, which is balance and gait disturbance. 5) Regarding the decision tree, all patients have been assumed to either deteriorate or remain stable without treatment. A minority of patients with NPH spontaneously improve. Another subgroup requires an ultra–low pressure valve to achieve adequate CSF drainage for improvement to be achieved; such patients would be poorly served by a standard shunt operation. 6) Calculations have been based on a 65-year-old patient with moderate dementia that is not defined in terms of the Mini-Mental State Examination score or an alternative. Sixty-five years is a relatively young age; there is no sensitivity analysis of the effect of age on their conclusions. 7) The mean QALY gain is 1.7 over a baseline of 1.4, but the authors assert that the responders (29\%) gain 6.2 each—a huge benefit. This means that the remaining 71\% must lose an average 0.14 QALYs—10\% of that expected. Thus the statement that “the average 65-year-old patient with suspected NPH is considerably more likely to benefit from shunt insertion than to suffer” is just not true—71\% can be expected to lose 10\% of their future QALYs. When there is such a bimodal benefit distribution, it is not appropriate to talk about an average patient; it is a mean benefit for the population being considered. 8) The authors’ use of a confidence interval is odd: it simply reflects the variability in expected benefit for cohorts of 1000 patients, which seems entirely arbitrary. The correct measure of uncertainty should take into account the possible error in the parameter inputs, which must be substantial for many of them.

The arguments advanced by Dr. Stein and colleagues are provocative but carry risk if they are followed blindly and not understood. Their study data should provoke the major grant-awarding agencies to fund randomized controlled trials or, at the very least, to create national registries akin to the United Kingdom Shunt Registry so that our understanding and management of one of the few remediable causes of dementia is put on a more secure foundation. Diagnostic criteria and outcome measures need to be refined. The role of cognitive enhancers can only be resolved by randomized controlled trials.\textsuperscript{8}

With regard to “blind” shunt insertion, it is reminiscent of the possibly apocryphal advice given to Simon de Montfort, the Earl of Leicester, who wanted to know how to distinguish Cathar heretics from nonheretics at the breaking of the siege of Béziers during the Albigensian crusade in 1209: “Caedite eos. Novit enim Dominus qui sunt eius.” (Kill them all. The Lord knows who are his own.)\textsuperscript{19} All the citizens were duly massacred.

References